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Addressing Race in Pulmonary Function Testing by Aligning Intent and Evidence With Practice and Perception

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The practice of using race or ethnicity in medicine to explain differences between individuals is being called into question because it may contribute to biased medical care and research that perpetuates health disparities and structural racism. A commonly cited example is the use of race or ethnicity in the interpretation of pulmonary function test (PFT) results, yet the perspectives of practicing pulmonologists and physiologists are missing from this discussion. This discussion has global relevance for increasingly multicultural communities in which the range of values that represent normal lung function is uncertain. We review the underlying sources of differences in lung function, including those that may be captured by race or ethnicity, and demonstrate how the current practice of PFT measurement and interpretation is imperfect in its ability to describe accurately the relationship between function and health outcomes. We summarize the arguments against using race-specific equations as well as address concerns about removing race from the interpretation of PFT results. Further, we outline knowledge gaps and critical questions that need to be answered to change the current approach of including race or ethnicity in PFT results interpretation thoughtfully. Finally, we propose changes in interpretation strategies and future research to reduce health disparities. CHEST 2022; 161(1):288-297

KEY WORDS: pulmonary function test; race or ethnicity; racial disparities; reference equations

Soon after John Hutchinson developed a spirometer (c. 1840) that was easier to deploy than its predecessors, he and others recorded the vital capacity of the lungs from a large number of people. The data showed that vital capacity increased with height, declined with age in adulthood, differed between sexes, and varied by occupation (eg, typesetter vs firefighter).[1]

Another early and consistent observation was that vital capacity varied between social classes.[1] Subsequently, descriptions ascribed to social class were overtaken by studies focused on capturing population differences by the sociopolitical construct of race.[2] Average vital capacity for the same sex, height, and age was reported to be lower in non-White compared with White groups. Although some investigators argued for

ABBREVIATIONS: PFT = pulmonary function test

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environmental sources for these differences—for example, early-life nutrition, respiratory illnesses, air pollution, exercise, and altitude—the mechanisms and quantification of these effects were not pursued systematically; rather, a narrative of innate differences took hold.[3]

The observed population differences in vital capacity were coopted and often used to justify and uphold slavery and structural racism in the United States.[4] Discriminatory practices were not limited to skin color, as a proclamation of these observed "innate" differences in lung function were used to deny the disability claims of Welsh vs English White miners.[5] In this social milieu where race and structural racism reinforced each other, and where race was thought to capture innate differences, clinicians and researchers incorporated race into their interpretation algorithms with the intent of improved prediction of expected lung function. Herein, we explore the consequences of embedding race in the interpretation of spirometry, highlight important considerations that influence interpretation strategies, and discuss challenges and alternatives to current practice.

Current Practice

Decades of epidemiologic studies have found that the extent to which lung function measured by spirometry is reduced compared with what is expected is associated with respiratory disease and death; notably, these associations also were observed for nonrespiratory disease and for overall mortality.[6-8] Pulmonary function tests (PFTs) show improvements in lung growth and attenuation in decline after reduction of harmful exposures such a smoking and air pollution.[9-11]

Spirometry results are reported as both an absolute number in the appropriate units—liters of air for vital capacity—and as a relative number compared with an expected value for a healthy, nonsmoking population of similar age, height, and sex. Consistent with widespread historical and current practice, guidelines recommend that expected values are calculated from equations derived in a representative population (ie, similar racial or ethnic identity) of otherwise healthy individuals.[12] Although this approach is distinct from the historic—and no longer recommended—practice of applying a correction factor for non-White populations to expected values derived from White populations, it still represents a form of so-called norming that requires critical re-evaluation. This approach relies on patient self-identity or the technologist's impression of someone's racial or ethnic background based on skin color or surname. Hundreds of reference equations have been published for different populations around the world. Current guidelines recommend using the spirometry equations from the Global Lung Function Initiative derived from large nonsmoking populations without respiratory conditions collected across multiple countries.[13] Figure 1 illustrates how observed mean differences in lung function across several racial and ethnic groups (Fig 1A) fall within the range of the observed variation within a single group (Fig 1B). Based on the lower observed lung function among non-White groups (Fig 1A), reference equations yield predicted values that are lower for non-White groups. Thus, for two people with the same absolute measure of lung function, the non-White individual will have a higher relative value (% predicted) compared with the White individual. The ratio of FEV_1 to FVC, which is central to the diagnosis of obstructive lung disease, does not depend on height in adults and is similar across race or ethnicity in both children and adults.[13] Some other PFT values, such as diffusing capacity and total lung capacity, also are found to be lower in most non-White groups, but unlike with spirometry, we do not routinely use race- or ethnic-specific equations. This is in part because of insufficient evidence, in that efforts to derive equations in non-White populations have been limited.[14-16]

The effects of reference equations are mitigated when an individual's lung function is measured before the onset of disease and longitudinal data are available. This holds true for individuals who are at high risk for a decline in adulthood or slower relative lung growth in childhood, such as for certain occupational exposures, before exposure to therapies with risk of pulmonary toxicity, in cystic fibrosis, or after lung transplantation. In these scenarios, large short-term changes or a longer-term decline in an adult's measured absolute lung function that exceeds what is expected from aging at a given height—in children, a deviation from the expected increase with growth—clinically is more informative than a single relative value. However, in the general case of how PFTs are used, a patient's lung function before disease onset usually is unknown.

Height as a Proxy for Chest Size: Relationships Between Physiologic and Epidemiologic Features

Vital capacity and many other core measurements of lung function are determined in part by the size of the

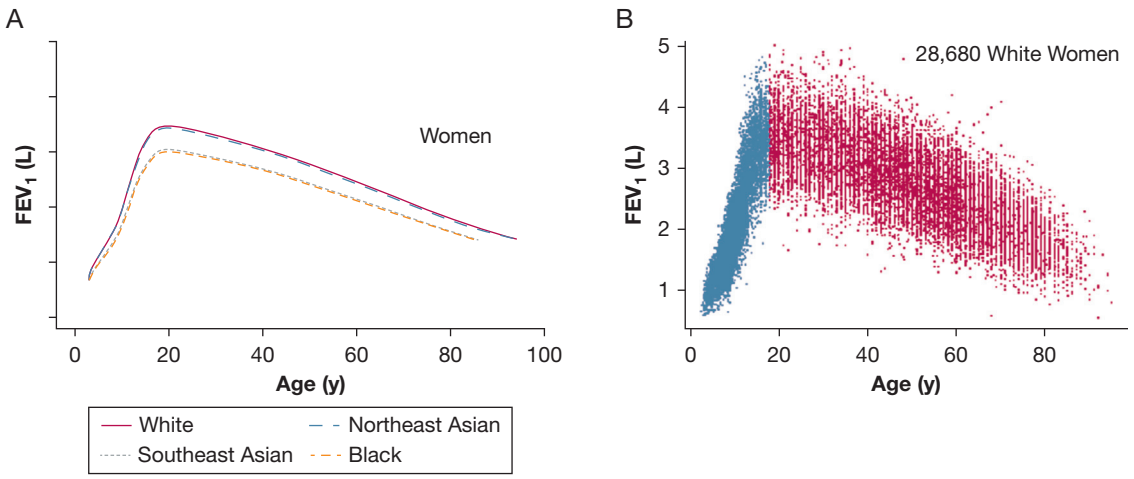

Figure 1 – *A, B, Graphs showing differences between vs within racial and ethnic groups. A, Data from the Global Lung Function Initiative (GLI) showing differences in FEV_1 between self-identified backgrounds at the same age and average height. (Reprinted with permission from Quanjer et al[13]) B, Data from GLI showing variation in FEV_1. About half of the scatter is accounted for statistically by differences in standing height. The remaining half of the variation remains large compared with the differences between backgrounds in (A). FVC follows the same trend as FEV_1, which leads to a similar ratio of FEV_1 to FVC between backgrounds.*

chest. Two people with the same standing height may not have the same chest size; hence, the wide variability in observed values in healthy populations. A fundamental question is whether lung function should be compared with healthy reference data by normalizing to standing height, as is the current practice, or measures more reflective of chest size such as sitting height. This distinction is relevant because multiple studies have shown differences in the proportion of sitting height to standing height between racial and ethnic categories.[17,18] The reasons for the observed differences may include technical difficulties and variation in measuring sitting height, but also likely overlap with factors that influence standing height, including early-life nutrition and genetics, and lung-specific factors, such as respiratory infections and exposures to indoor and outdoor pollution, physical activity, and high altitude.[19-22]

The use of sitting height instead of standing height reduces lung volume differences between Black and White populations by up to 50%[17,23]; larger effects have been seen for racial differences in children[24] and lesser or no impact has been seen in Asians.[25] These and other studies also found that socioeconomic variables such as composite measures of poverty and immigration status account for some, but not all, residual differences between racial and ethnic groups.[26] More detailed measurements of the chest to estimate surface area or volume have been reported to reduce the difference between populations even more, by up to 90%.[25,27]

Using sitting height in place of standing height yields a more accurate value for expected lung function by which to assess the likelihood of disease. When considering the research implications of a change to using sitting height, we also must recognize that childhood illness, nutrition, and the cumulative physiologic effect of social and environmental stressors—by way of direct vs indirect pathways such as the cumulative effect of life stressors (allostatic load) and epigenetics—may impact leg length and chest size differentially, a concept also supported by small secular trends in body proportions.[28-30] Thus, although using sitting height can reduce relative lung function differences between racial and ethnic categories, it may lead to relative values that seem closer to normal and mask the impact of social determinants on lung function. The same reasoning applies to more detailed measurements of chest volume and stiffness, distensibility of the airspaces, and respiratory muscle strength, because these are the physiologic mechanisms by which all external and genetic inputs influence lung function.

Genetic Contributions to Lung Function and PFT Interpretation

Genetic contributions to physiologic determinants, including gene-environment interactions, also are expected to influence lung function trajectory.[22,31] Inclusion of global genetic ancestry captures some of the differences between observed lung function and that predicted by reference data specific for self-identified race, even beyond what is achieved through the use of sitting height and select socioeconomic variables; the effect is similar to or smaller than the expected

differences between populations.[32,33] Global genetic ancestry moves toward a direction of understanding genetic risk, but has been illustrated as a weak predictor of whether specific polymorphisms are present. In addition, because genetic ancestry is associated with self-identified race,[34] its use is subject to the same risks of norming lung function and masking modifiable social risk factors. The inclusion of genetic ancestry in PFT results interpretation is not a ready solution to the concerns with using race and ethnicity in PFT interpretation. Promisingly, single nucleotide polymorphisms are associated with lung function decrements, thereby supporting some component of genetic determinism for lung function.[35,36] However, we currently have only superficial knowledge; polygenetic risk scores to date largely have been derived in White populations, and this information is not yet practical for patients requiring PFTs in the clinical setting. Although this approach would not resolve the observed differences in lung function between racial and ethnic groups, capturing genetic risk may allow us to quantify better the contribution of socioenvironmental factors that previously were hidden by inclusion of race or ethnicity in reference equations.

Arguments Against Using Race-Specific Equations

Race is a sociopolitical construct, and calls have been made to eliminate its use as a proxy for biology.[37] Its use in PFT results interpretation is fraught with limitations. In current practice, we have no mechanisms for defining predicted lung function for groups not included in the major reference equations, for individuals of multicultural (or multiracial) backgrounds, or for immigrant populations.[38] Race does not capture many other factors, such as obesity, childhood respiratory infections, or smoking, which are associated with differences in lung function and are not considered routinely during interpretation.[39-42] Socioeconomic background is associated with lung function independent of race[43]; the use of race-specific equations in clinical practice and research may mask potentially modifiable risks for reduced lung function and disease, including mediators among early-life nutrition, sanitation, pollution, income, and education.[17,21,26,42,44-47] Race does not accurately capture individual differences in the exposures and genetics that lead to variation in lung function at the same age, standing height, and sex. Figure 1B shows an example of the large variation within a race.

Race-specific equations applied to most non-White groups lead to a higher relative value (eg, percentage of predicted) for the same absolute measurement in a person of the same age, sex, and height as a White person (Table 1). Concern exists that this practice may increase the risk of a poor outcome from underdiagnosis of respiratory disease (Table 2). Most research articles that form the evidence base for lower lung function in non-White populations did not examine structural or social determinants of health or environmental exposures.[48] Omitting the use of race in PFT results interpretation potentially would motivate investigations to understand better the sources of lung function differences and disease disparity, to remove barriers to care, and to improve health care equity.

One assumption in these concerns is that it should not be typical in health for two people of the same sex and similar age and height to have a difference in a lung function measurement. In support of this idea, after adjustment for age and standing or sitting height, one study found more similar survival rates between Black and White individuals with the same FVC when not adjusting for race.[65] In another large cohort, the association between FEV_1 and mortality was independent of race.[66] Further investigation is required to determine if there is a mechanistic relationship between lung function and survival and whether they might be influenced by the same factors independently.

Concerns About Ignoring Race

An alternative to using race is to use a range of values that includes individuals across many global populations while continuing to adjust for sex, age, and height. This would provide a predicted value that represents a diverse population average but will widen the limits of normal that can be expected in otherwise healthy people. This approach may miss pathophysiologically reduced lung function in some individuals while resulting in overtesting and diagnosis in others (Table 2); we do not know the extent to which this error would differ from current practice where lung function that is mildly abnormal compared with an expected value often is not associated with disease. Under this new approach, continued use of previous cutoffs for interpretation may mean that an individual's results will be viewed as reduced and some life-saving therapies—including chemotherapy, lung cancer resection, and bone marrow transplantation for blood malignancies—that take into consideration lung function when determining candidacy would be withheld, further perpetuating racial

TABLE 1] Different Assessments of Lung Function at Three Different FEV_1, FVC, and FEV_1 to FVC Ratio Measurements Depending on Which Race- or Ethnic-Specific GLI Prediction Equation is Used

	FVC		For FVC = 1.5, 2.5, 3.5	
GLI Group	Predicted (L)	LLN (5th centile)	% Predicted	*Z* Score
White	3.78	2.98	40, 66, 93	−4.93, −2.66, −0.56
Black	3.23	2.49	46, 77, 108	−4.00, −1.63, 0.58
Northeast Asian	3.68	3.03	41, 68, 95	−5.79, −3.02, −0.45
Southeast Asian	3.25	2.53	46, 77, 108	−4.16, −1.71, 0.57
Other/mixed	3.48	2.78	43, 72, 101	−4.86, −2.31, 0.06
	FEV_1		For FEV_1 = 1.0, 2.0, 3.0	
White	3.03	2.38	33, 66, 99	−4.90, −2.58, −0.07
Black	2.61	1.99	38, 77, 115	−4.10, −1.62, 1.07
Northeast Asian	2.98	2.35	34, 67, 101	−4.92, −2.54, 0.04
Southeast Asian	2.68	2.07	37, 75, 112	−4.29, −1.81, 0.86
Other/mixed	2.82	2.21	35, 71, 106	−4.68, −2.20, 0.49
	FEV_1 to FVC Ratio		For FEV_1 to FVC Ratio = 0.5, 0.7, 0.9	
White	0.81	0.70		−3.79, −1.61, 1.66
Black	0.81	0.71		−3.93, −1.71, 1.62
Northeast Asian	0.81	0.72		−4.50, −1.99, 1.78
Southeast Asian	0.83	0.74		−4.54, −2.18, 1.38
Other/mixed	0.82	0.72		−4.17, −1.86, 1.61

In the example, for a 47-year-old woman who is 167.5 cm tall (5 feet, 6 inches), differences in relative values exist that may be small when compared with other unaccounted sources of variation in lung function and limitations in interpretation based on thresholds. GLI = Global Lung Function Initiative; LLN = lower limit of normal.

and ethnic health disparities. Similarly, admission to some occupations might be limited.

Limitations of PFTs and Reference Values That Place Concerns About Race in Perspective

High repeatability and reference values gives PFTs an objectivity and authority that can lead to overinterpretation and misuse of the results at an individual patient level. An overreliance on limits of normal, or cutoffs for disease or disability classification, ignores that the variability in lung function observed between healthy, nonsmoking people with no respiratory symptoms—within or between populations—is very wide. When lung function is reduced severely, the choice of reference populations is less likely to change the interpretation of the results. When the results lie closer to the lower limit of normal, a greater degree of uncertainty exists. That is, values slightly above or below a threshold have similar meaning; however, they are labeled normal or abnormal in the commonly used binary interpretation. A misplaced emphasis on the percentage below the predicted value ignores comorbid conditions, exposures, and treatments that contribute to differences in lung function.

PFTs reflect limited types of function and structural changes, and thus their relationship to symptoms and a patient's ability to perform activity is imperfect. Many people with lung function measurements that lie within the expected range have significant respiratory symptoms or smoking history; in others, early or mild manifestations of lung disease often are missed. Outside of specialized areas such as swimming and diving or with advanced age, physical health and exercise capacity are independent of lung function when lung function is in the normal range of values.[67-69] Strict cutoffs for PFT results ignore these limitations and need to be reconsidered (Table 2).

Reference values from one geographic region and period may not reflect the genetic mix, exposures, and nutritional status of the populations in which they are used.[70] Notably, the Global Lung Function Initiative reference equations used data from Black Americans, but no other African populations, and comparative studies since its publication show that it is does not reflect expected lung function for all African

TABLE 2] Concerns About the Use of Race in Interpretation of PFTs

Variable	Limitations and Considerations	Knowledge and Practice Gaps
General concerns with using race in medicine		
Does not capture many of the relevant environmental influences on lung function	• Needed to discover mechanisms for differences and to suggest societal interventions[49]	• Mechanisms leading to differences in lung function
Does not capture acculturation, mixed ancestry		
Not a proxy for an individual's genetics	• Race captures some genetics	• Better genetic information
May bias inclusion in clinical trials	• Can be used to identify disparities	• Sources of disparities
May perpetuate health disparities	• Risk and treatment prediction may sometimes be improved with race	• Sources of difference in risk and treatment response
Sociopolitical construct that supports structural racism		
Concerns with using race in PFT interpretation		
For individuals near a threshold, potential for: Delayed diagnosis Withheld treatments	• Overreliance on lung function thresholds without data to support such use	• Outcomes-based standards rather than comparison with reference populations
Restricted access to: Disability	• Weak relationship between lung function and work ability[50] • Variable use of race in guidelines[51,52]	• Variation in disability requirements across states, insurers • Relationship between pulmonary function and ability to work
Home assisted ventilation	• Criteria not validated[53]	
Rehabilitation programs	• Pulmonary function not always related to potential benefit[54-56]	• Variation in requirements across insurers
Lung transplantation	• Referral guidelines do not rely on a single threshold[57,58]	• Whether transplant referral delayed
Concerns with not using race in PFT interpretation		
For individuals near a threshold, potential for: Over-diagnosis: unnecessary testing, treatments with potential side effects, anxiety	• FEV_1 to FVC ratio is important for diagnosis of obstructive lung disease and similar between racial and ethnic categories	• Education about limitations of thresholds and reference values, particularly to detect mild disease
Ineligible to be a firefighter, commercial diver, or miner[59,60]	• Variable use of PFTs, thresholds, and race across employers • Additional evaluation can override PFTs for eligibility	• Relationship between pulmonary function and job performance and risks not established[64] • How many candidates affected and feasibility of further evaluation
Withholding of certain treatments: Chemotherapy Lung cancer resection[61] Bone marrow transplant[62]	• Data to question the practice[63]	• Availability of secondary testing such as exercise tests
Higher life-insurance premiums for non-Whites	• Race commonly not considered for D_{LCO} on PFT reports	
For Whites, a race-composite reference may lead to lung function too high to qualify for certain interventions and disability	• Overreliance on lung function thresholds	

D_{LCO} = diffusing capacity of the lung for carbon monoxide; PFT = pulmonary function test.

populations.[71,72] Beyond minimal smoking history and absence of a respiratory condition, the extent to which we should limit other factors that influence lung function such as obesity and nonsmoking exposures in the definition of healthy is not clear. For some tests such as the diffusing capacity or tests of respiratory muscle strength, even reference datasets all derived in White populations differ from one another by a very large amount.[73-75]

Bias in Pulse Oximetry Highlights Differences Between Measurement and Interpretation

The COVID-19 pandemic has raised awareness of the systematic bias of pulse oximetry in individuals with darker skin tones.[76] Some, but not all, models of pulse oximeters report higher values with increasing skin pigmentation.[77,78] This measurement problem is the result of calibration of light transmission through darker skin based only on light-skinned individuals. This overestimation of blood oxygenation may lead to delayed recognition of more severe disease. Although the use of race in PFT results has similar implications for delayed recognition of disease in Black individuals, the underlying problem with PFTs is not one of measurement. PFTs provide a direct measurement, and thus, our focus is not on developing a better device. We need to address the assumptions made when interpreting results with reference equations.

Aspirations and a Practical Path Forward

It is time for the interpretation of PFT results to reflect our overall intention to improve health. This requires us to acknowledge the history of how interpretation has been used to favor majority populations, to recognize implications of language when describing differences in function, and to examine critically past and future unintentional consequences of the improper use of race or ethnicity. Reporting through race-based algorithms in the PFT laboratory risks portraying racial disparities as innate and immutable.[79] By anchoring on the improved prediction of lung function from race- or ethnic-specific reference equations, we miss how the significant residual variation still leaves much uncertainty about the expected value for an individual.

One path forward is to use a common set of reference equations derived from a composite population inclusive of individuals from many racial and ethnic backgrounds. A practical option to achieve this already exists for spirometry through the race-composite set of equations from the Global Lung Function Initiative (labeled "Other"). Although this option is limited because it averages only across the four racial and ethnic groups in Figure 1, it does offer an opportunity not to select a race-specific prediction equation. A counterargument to this proposal is that it opens the door for individual clinicians and policies to use race downstream in variable ways with unpredictable consequences. Yet, when viewed as a product of structural racism and a form of explicit bias, no calculation of net good or harm justifies the continued use of race. An urgent need exists to identify and use the variables for which we take race as a proxy and develop more accurate and unbiased interpretation algorithms. Only then can we unveil what race is hiding.

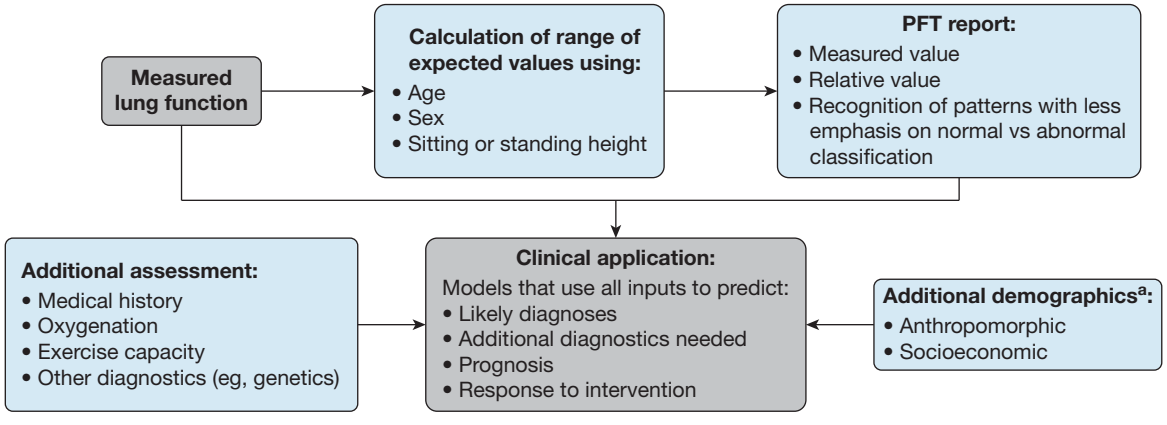

Figure 2 – *Diagram showing a proposed approach to include PFTs with other factors into clinical decisions. This approach allows clinicians and patients to appreciate the limitations of interpretation based on comparison to reference values and to frame the role of PFTs in decision-making relative to other data about the patient. Multivariate models allow for a Bayesian approach where the inputs capture probabilities of outcomes before PFTs and the output provides probabilities after PFTs, rather than an normal-abnormal dichotomization of PFT results based on fixed thresholds. *Use of race can help to identify health inequities and to ensure broad inclusion in research. PFT = pulmonary function test.*

Also opportunities exist to reduce the influence of race or ethnicity downstream of the PFT laboratory. Multivariate clinical prediction models may lessen the impact of the exact value of one variable (Fig 2). These models must be developed using data from populations representative of the individuals to which they will be applied. The models can include demographics, symptoms, medical history, and the results of other tests and treatment responses. A cutoff will still need to be applied to the resulting multivariate score to make a clinical decision, but it would be more holistic than applying a cutoff to individual PFT results. In the clinic, the clinician and patient can discuss the determinants of lung function and limitations in our ability to calculate expected values for an individual. Both clinician and patient can learn how the relationships among PFTs, disease, and response to therapeutics are weaker the closer the results are to expected values and that other factors must be considered in addition to single measurements. Prediction models can be developed to focus on outcomes such as prognosis and the likelihood of benefitting from a medication or intervention. For some outcomes, lung function may not have sufficient explanatory power compared with other inputs and will be removed from the model, as is occurring for the lung transplantation allocation score.[80] Research should continue to ascertain and use race, not as an explanatory variable, but rather in a manner that highlights where racial health disparities exist, that reduces enrollment bias, and that maximizes the generalizability of the results.[49]

Beyond agreeing on a solution, we must educate the world to use PFT data more thoughtfully. We must examine critically systems that rely heavily on lung function thresholds in isolation through research that builds the evidence base for more holistic models, revised guidelines that stop using lung function thresholds, and educational efforts not only within the pulmonary community, but toward external agencies as well. Changing practice will necessitate engaging disability offices, insurers, employers, policy makers, and patients; many are not aware of the bias that exists. We need this discussion to be applicable at a global level and need leadership of all national and international respiratory bodies to take this issue on as a matter of priority.

The increased attention on structural racism and use of race in medicine is an opportunity for the pulmonary community to be a part of a new social milieu in which we aim to remove race from the interpretation of PFT results and understand the true determinants of lung health. Despite the challenges and evidence gaps noted, opportunities exist to align intent and practice with impact and perception. To have the most benefit, changes to PFT interpretation and application must be paired with elimination of racial inequities in access and delivery of health care.

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